REMARKS

Status of Claims

Claims 24-28 have been newly added. Thus, claims 1-28 are now pending. Claims 1-19 and 22 were withdrawn from consideration by the Examiner as being drawn to a nonelected invention. Claims 20, 21, 23 and 24-28 are under consideration.

Amendments to the Claims

Claim 20 has been amended and new claims 24-28 have been added in order to create separate claims for methods for the diagnosis of acute cardiovascular diseases, for the prognosis of acute cardiovascular diseases, and for the monitoring of therapies of acute cardiovascular diseases. Previously, claims 20 and 23 encompassed all of these methods. Specifically, claim 20 has been amended to remove the phrase "for the diagnosis or prognosis of acute cardiovascular diseases." As a consequence, claim 20 is now only directed to a method for the monitoring of therapy of acute cardiovascular disease. Claims 20 and 23 have also been amended to improve the language of the claims. New claims 25 and 26 are directed to a method for determining the prognosis of acute cardiovascular disease. New claims 27 and 28 are directed to a method for the diagnosis of acute cardiovascular disease. As such, the new claims all fall within the elected Group III ("drawn to therapeutic methods monitoring acute cardiovascular diseases;" *see* Office Action mailed June 10, 2009, at page 3). Support for the claim amendments and the new claims may be found throughout the specification, for example, on page 13, 1st full ¶ and last ¶, on page 15, 1st ¶, and from page 22, last ¶, to page 25, 1st full ¶. New claim 24 is directed to a method for the monitoring of therapy of acute cardiovascular disease for a specified time period of 6 months. Support for this

new claim may be found, for example, in Examples 3a and 2b. Thus, all of the claim amendments and the new claims are fully supported by the specification and do not add any new subject matter.

Rejections under 35 U.S.C. §102 - Novelty Requirement

Claims 20 and 23 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Bayes-Genis et al. (The New England Journal of Medicine 345(14):1022-1029 (2001)) ("Bayes-Genis"). Office Action, page 4. Specifically, the Office contends that Bayes-Genis discloses methods of measuring PAPP-A in acute coronary syndromes and that PPAP-A was found to be a marker for acute coronary syndrome. Applicants respectfully traverse for the following reasons.

As a consequence of the claim amendments, currently pending claim 20 is directed to a method for the monitoring of therapy of acute cardiovascular disease. In the context of the present invention, "monitoring of the therapy" relates to controlling and, optionally, adjusting the therapeutic treatment for an individual. The "therapeutic treatment" includes all treatments that possibly improve the pathophysiological condition of an individual, including, for example, the administration of pharmaceutical agents (e.g. the glycoprotein IIb/IIIa-inhibitor abciximab) as well as surgical or physically invasive treatment (e.g. balloon dilatation) (*see, e.g.*, specification at page 15, 1st ¶). Markers that are useful for the diagnosis of a disease do not necessarily allow controlling or adjusting the therapeutic treatment of a patient and thus are not necessarily useful for monitoring of the therapy of that disease. The instant specification teaches, based on experimental evidence, that the therapeutic treatment of a patient can be controlled or adjusted according to the PAPP-A status (*see, e.g.*,

specification at section "III. PAPP-A and Combinations," pages 46 to 54). Bayes-Genis does not teach, neither expressly nor inherently, using PAPP-A as an inflammatory marker for the monitoring of therapy of acute cardiovascular disease. However, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); M.P.E.P. § 2131. Thus, because Bayes-Genis does not teach every element of amended claim 20, it cannot anticipate the claim. Because claim 23 depends from claim 20, Bayes-Genis therefore also cannot anticipate claim 23. New claims 25 and 26 are directed to a method for determining the prognosis of acute cardiovascular disease. In the context of the present invention, "prognosis" relates to the prediction of the probability (in %) whether an individual will suffer from a particular cardiovascular event. Markers that are useful for the diagnosis of a disease do not necessarily allow the prediction of the probability (in %) whether an individual will suffer from a particular cardiovascular event and thus are not necessarily useful for determining the prognosis of acute cardiovascular disease. The instant specification identifies, based on experimental evidence, PAPP-A as an independent predictive marker for the outcome for patients in the months subsequent to the diagnosis of acute cardiovascular disease (*see, e.g.*, specification from page 22, last ¶, to page 25, 1st full ¶). Thus, the instant invention teaches PAPP-A not only as a diagnostic marker, but also as a predictive marker that allows determining the prognosis of acute cardiovascular disease. For example, such prognosis can be determined even after the occurrence of an acute ischemic event that is caused by atherosclerotic plaque instability.

Bayes-Genis does not teach, neither expressly nor inherently, using PAPP-A as an inflammatory marker for determining the prognosis of acute cardiovascular diseases. Thus, because Bayes-Genis does not teach every element of new claims 25 and 26, it cannot anticipate the claims.

New claims 27 and 28 are directed to a method for the diagnosis of acute cardiovascular diseases comprising determining the concentration of at least one inflammatory marker selected from soluble CD40-ligand (sCD40L) and PlGF. Bayes-Genis also does not teach, neither expressly nor inherently, using sCD40L and/or PlGF as inflammatory marker(s) for the diagnosis of acute cardiovascular diseases. Thus, because Bayes-Genis does not teach every element of new claims 27 and 28, it cannot anticipate the claims.

Applicants therefore respectfully submit that amended claims 20 and 23 (and the new claims 25-28) are not anticipated by Bayes-Genis and request withdrawal of the rejection under 35 U.S.C. §102(b).

Rejections under 35 U.S.C. §103 - Nonobviousness Requirement

Claims 21 is rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Bayes-Genis in view of Corsini et al. (Pharmacology & Therapeutics 84:413-428 (1999)) ("Corsini"). Office Action, page 4. The Office acknowledges that Bayes-Genis does not specifically teach the administration of statins as a therapeutic vascular agent to a patient. *Id.* The Office contends, however, that Corsini teaches procedures for administering statins to patients and the effects of statins in ameliorating vascular atherosclerosis and reducing cardiovascular-related morbidity and mortality in patients. *Id.* at page 5. The Office concludes that it would have been obvious to one of skill in the

art to treat the detected vascular patients of Bayes-Genis with the statins of Corsini. *Id.* Applicants respectfully traverse for the following reasons.

As a consequence of the amendment of claim 20, claim 21 is now directed to a method for the monitoring of therapy of acute cardiovascular disease, wherein the therapy comprises the administration of at least one of statins and inhibitors of the glycoprotein IIb/IIl-receptor. As explained in the Novelty Requirement section above, Bayes-Genis does not teach using PAPP-A as an inflammatory marker for the monitoring of therapy of acute cardiovascular disease. Corsini also does not teach using PAPP-A as an inflammatory marker for the monitoring of therapy of acute cardiovascular disease, and therefore Corsini cannot make up for the deficiencies of Bayes-Genis. Thus, neither Bayes-Genis or Corsini alone nor their combination provides any disclosure regarding the use of PAPP-A as an inflammatory marker for the monitoring of therapy of acute cardiovascular disease. One of ordinary skill in the art would therefore have no good reason or motivation to attempt using PAPP-A for this purpose. Furthermore, one of ordinary skill in the art would have no reasonable expectation of success in using PAPP-A for this purpose, and using PAPP-A for this purpose would not yield predictable results.

Based on the Supreme Court's decision in *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1734 (2007), the Office has announced seven exemplary rationales that may support a conclusion of obviousness set forth in M.P.E.P. § 2143. All of these bases for obviousness require that one of ordinary skill in the art, without knowing anything of the claimed invention, would not only have a reason to produce that invention, but also would have a reasonable expectation of success and achieve predictable results. Since

these requirements are not met in the instant case, Applicants submit that there is no *prima facie* case of obviousness for claim 21.

Whether Corsini teaches procedures for administering statins to patients and the effects of statins in ameliorating vascular atherosclerosis and reducing cardiovascular-related morbidity and mortality in patients, as contended by the Office, does not change this conclusion.

In view of the above, Applicants respectfully request that the rejection of claim 21 under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

In view of the foregoing remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims. If the Examiner believes a telephone conference would be useful in resolving any outstanding issues, the Examiner is invited to call the undersigned at (202) 408-4316.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: June 25, 2010

By: _____
Marcus D. Kretzschmar
Reg. No. 63,815